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The expression of cell adhesion molecule 1 and its splicing variants in Sézary cells and cell lines from cutaneous T-cell lymphoma

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Short title

CADM1 expression in Sézary syndrome

Abbreviations

cell adhesion molecule-1 (CADM1), tumor suppressor lung cancer-1 (TSLC1), Sézary syndrome (SS), mycosis fungoides (MF), adult T-cell leukemia/lymphoma (ATLL), anaplastic large cell lymphoma (ALCL), C-C chemokine receptor type 4 (CCR4), human T-cell leukemia virus 1 (HTLV-1), peripheral blood mononuclear cell (PBMC), cutaneous T-cell lymphoma (CTCL), diffuse large B-cell lymphoma (DLBCL), enzyme-linked immunosorbent assay (ELISA), reverse transcriptase-polymerase chain reaction (RT-PCR)

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ABSTRACT

Cell adhesion molecule 1 (CADM1) is aberrantly expressed by T-cell neoplasms such as adult T-cell leukemia/lymphoma (ATLL) and mycosis fungoides (MF). We studied the expression of CADM1 and its splicing variants in Sézary syndrome (SS), MF, other cutaneous T-cell lymphoma (CTCL), and cell lines derived from T- and B-cell lymphomas. Soluble CADM1 was measured in the patients' sera. CADM1+ cells in the blood and skin lesions were examined by flow cytometry and immunostaining, respectively. Soluble CADM1 was measured by ELISA, and the splicing variants of *CADM1* transcripts were determined by reverse transcriptase-polymerase chain reaction, followed by sequencing. As a result, circulating CADM1+ cells were significantly increased in 7 of 10 patients with SS, ranging from 7.9% to 74.5% of the CD3+CD4+ fractions (median; 33.7%) (cut off value; 6.5%). The percentages of CADM1+ cells were usually less than those of circulating Sézary cells. CADM1 was expressed, to various degrees, in 6 of 9 T-cell lines derived from SS, MF, ATLL, and anaplastic large cell lymphoma (ALCL), but negative in B-cell lymphoma-derived cell lines. CADM1+ cells were present in the skin infiltrates of MF, SS, ATLL and ALCL. Serum levels of soluble CADM1 were not significantly elevated in SS/MF. Three major splicing variants of CADM1 expressed by neoplastic T cells contained different

71 combinations of the exons 7, 8, 9 and 11, including a putative oncogenic variant
72 composed of exons 7-8-9-11. In conclusion, CADM1 is frequently expressed in Sézary
73 cells and cell lines from CTCL.
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75 **Keywords**

76 CADM1, Mycosis fungoides, Sézary syndrome, splicing variant, T-cell lines,
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